II. REMARKS

Formal Matters

Claims 1-29 are pending after entry of the amendments set forth herein.

Claims 1-4 and 19-22 were examined and were rejected. Claims 5-18 and 23-28 were withdrawn from consideration.

Claims 1 and 4 are amended. The amendments to the claims were made solely in the interest of expediting prosecution, and are not to be construed as an acquiescence to any objection or rejection of any claim. Support for the amendments to claims 1 and 4 is found in the claims as originally filed, and throughout the specification, in particular at the following locations: page 6, lines 30-35; page 12, line 11 to page 13, line 10; and page 14, lines 5-30. Accordingly, no new matter is added by these amendments.

Claim 29 is added. Support for new claim 29 is found in the claims as originally filed, and throughout the specification, including the following exemplary locations: page 14, lines 31-33. Accordingly, no new matter is added by these new claims.

Applicants respectfully request reconsideration of the application in view of the remarks made herein.

Examiner Interview

The undersigned Applicants' representative thanks Examiner Jiang and Examiner Padmanabhan for the courtesy of a telephonic interview which took place on March 30, 2004, and which was attended by Examiners Jiang and Padmanabhan, inventor Dr. Karl Weisgraber, and Applicants' representative Paula A. Borden.

During the interview, the rejection of claims 1-4 and 19-22 under 35 U.S.C.§ 102(a), was discussed.

Rejection under 35 U.S.C.§102(a)

Claims 1-4 and 19-22 were rejected under 35 U.S.C.§102(a) as allegedly anticipated by Scolnick (WO 95/06470). The Office Action stated that claims 1-4 and 19-22 were rejected over Scolnick for reasons of record stated in the Office Action dated March 18, 2003.

Comments regarding the instant invention as claimed

Claim 1 recites a pharmaceutical composition comprising (a) an agent that binds specifically to apolipoprotein E4 (apoE4) and disrupts domain interaction within the apoE4 protein, thereby reducing domain interaction by at least about 10%; and (b) a pharmaceutically acceptable excipient.

ApoE contains two structural domains: an amino-terminal domain and a carboxyl-terminal domain. Each domain is associated with a specific function. The amino-terminal domain contains the lipoprotein receptor binding region; and the carboxyl-terminal domain contains the major lipid-binding elements. The two domains appear to interact with each other in an isoforms-specific manner, a phenomenon known as "domain interaction." Domain interaction is responsible for the preference of apoE4 for very low density lipoproteins. The properties of apoE4 are associated with various pathologies, including Alzheimer's Disease. The present invention provides compounds that bind to apoE4 and reduce domain interaction. Such compounds therefore effect a change in the conformation of apoE4 from a pathological conformation to a non-pathological conformation.

Scolnick cannot anticipate the instant invention as claimed.

The final Office Action stated: 1) Scolnick discloses that a HMG-CoA reductase inhibitor, a statin such as lovastatin, simvastatin, pravastatin, and fluvastatin, being an agent that specifically reduces apolipoprotein E4, is useful in a composition to be administered or a pharmaceutical formulation; and 2) these statins are known to have molecular weights in a range within the instant claim. The Office Action concluded that Scolnick anticipates the claimed invention. Applicants respectfully traverse the rejection.

It is basic patent law that in order to anticipate a claim, a reference must teach each and every element of the claim. *Verdegaal Bros. v. Union Oil of California*, 2USPQ2d 1051, 1053 (Fed. Cir. 1987).

Scolnick neither discloses nor suggests an agent that specifically binds to apoE4 and disrupts domain interaction within the apoE4 protein, thereby reducing domain interaction by at least about 10%. Accordingly, Scolnick cannot anticipate the instant invention as claimed.

Scolnick discusses statin compounds. The statin compounds discussed in Scolnick inhibit HMG CoA reductase. HMG CoA reductase is an enzyme that is unrelated in amino acid sequence and structure to apoE4. There would be no reason for a person skilled in the art to believe that a statin would even bind specifically to apoE4, much less inhibit apoE4 domain interaction.

"Intended use"

The final Office Action stated that it is well settled that "intended use" of a composition or product, e.g., "specifically reduces apolipoprotein E4 domain interaction by at least about 10%" will not further limit claims drawn to a composition or product. However, the ability to reduce apoE4 domain interaction is a property of the recited agent, not an "intended use." Indeed, the final Office Action acknowledged that the recitation of "specifically reduces apoE4 domain interaction" is a property of the recited agent.

The final Office Action cited *Ex parte Masham* 2 USPQ2d 1647 (BPAI, 1987); and *In re Hack* 114 USPQ 161 (CCPA, 1957) in support of the position that an intended use does not further limit claims drawn to a composition or product. However, as discussed below, the cited cases are not relevant to the rejection of the instant claims.

In *Ex parte Masham*, the rejected claim recited an apparatus for mixing flowing developer material, including means for receiving the flowing developer material and mans for mixing the flowing developer material, said mixing means being stationary and completely submerged in the developer material. The claim was rejected as anticipated by a reference that disclosed an apparatus that satisfied the structural requirements of the claims apparatus. The Board agreed with the examiner's position that the recitation "completely submerged in the developer material" does not impose any structural limitations upon the claimed apparatus which differentiates it from that disclosed in the prior art reference. In *Ex parte Masham*, a comparison of the prior art apparatus and the claimed apparatus revealed that the claimed apparatus was not structurally different from the prior art apparatus. In contrast, a recitation of "binds specifically to apoE4 and disrupts domain interaction within the apoE4 protein, thereby reducing domain interaction by at least about 10%" does indeed impose structural limitations upon the recited agent, which structural limitation is possessed by the compounds discussed in Scolnick.

In *In re Hack*, the rejected claims recited a brazing alloy composed of recited percentages of gold, copper, and nickel. The claims were rejected over art that disclosed alloys of gold, copper, and nickel. The Court stated that the reference in the claims to "brazing" is but an indication of the broad filed of contemplated use and is not a limitation to be considered in the question of patentability. In *In re Hack*, a comparison of the claimed composition reciting specific percentages of gold, copper, and nickel with prior art compositions revealed no differences in the compositions. In contrast, a recitation of "binds specifically to apoE4 and disrupts domain interaction within the apoE4 protein, thereby reducing domain interaction by at least about 10%" does indeed impose structural limitations upon the recited agent, which structural limitation is possessed by the compounds discussed in Scolnick.

It is unclear why Scolnick has been cited as anticipating the instant claims, as the compounds discussed in Scolnick bear no relationship whatsoever to the instant compositions as claimed. The compounds discussed in Scolnick inhibit HMG CoA reductase. HMG CoA reductase is a protein that is unrelated to apoE. The compounds discussed in Scolnick do not bind apoE, nor would such compounds be expected to bind apoE. There is no disclosure or suggestion in Scolnick that the compounds discussed in Scolnick possess the property of reducing apoE4 domain interaction, nor would such compounds be expected to reduce apoE4 domain interaction. Accordingly, Scolnick cannot anticipate the instant invention as claimed.

The Office Action has apparently selected Scolnick as a reference to cite in the instant application solely on the basis of Scolnick's disclosure that statins lower apoE4 levels in the central nervous system. However, a disclosure that an agent lowers apoE4 levels is not sufficient to warrant an anticipation rejection of the instant claims.

"Inherency anticipation"

The final Office Action stated that the recitation of "specifically reduces apolipoprotein E4 domain interaction by at least about 10%" is a property of the recited agent, and further stated that "it has been well settled that recitation of an inherent property of a composition or an agent will not further limit claims drawn to a composition or an agent." Final Office Action, page 3.

According to the law, a reference may anticipate a claim even if a feature recited in the claim is not specifically disclosed in the reference. However, where the reference is silent as to a specific

limitation in the claims, such a gap in the reference must be filled with recourse to extrinsic evidence in order for the reference to serve as an anticipatory reference by inherency. Such evidence must make clear that the missing descriptive matter is *necessarily* present in the thing described in the reference, *and that it would be so recognized by persons of ordinary skill in the art* at the time the invention was made.[1] The characteristic must flow *undeniably and irrefutably* from the express disclosures of the prior art reference. Mere possibilities or even probabilities are not enough to support a finding of anticipation.[2]

As discussed in the MPEP §2112, in relying upon a theory of inherency, **the examiner must provide a basis in fact and/or technical reasoning** to reasonably support the determination that the allegedly inherent characteristic *necessarily* flows from the teachings of the applied prior art.[3]

The Office has provide no basis in fact and/or technical reasoning that a statin compound as discussed in Scolnick binds specifically to apoE4 and disrupts domain interaction within the apoE4 protein, thereby reducing domain interaction by at least about 10%, as recited in claim 1. Indeed, in view of the fact that HMG CoA reductase and apoE4 are completely unrelated proteins, there would be no reason for a person skilled in the art to expect that a statin compound that inhibits HMG CoA reductase would even specifically bind apoE4, much less inhibit apoE4 domain interaction. Accordingly, the Office has not established a case of inherency anticipation.

"Mechanism of action"

The final Office Action stated "the mechanism of action of a treatment does not have a bearing on the patentability of the invention even though applicant has proposed or claimed the mechanism." Final Office Action, page 3.

As discussed above, Scolnick states that the statin compounds discussed therein lower apoE4 levels in the central nervous system (CNS). As Dr. Weisgraber explained during the telephone interview, the instant claims do not recite lowering apoE4 levels. Instead, the agents **disrupt apoE4**

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[1] *Continental Can Co. USA, Inc. v. Monsanto Co.*, 20 USPQ2d 1746, 1749-1750 (Fed. Cir. 1991). In this case, a summary judgement of inherency anticipation was deemed improper because of a material fact issue whether a prior art reference's process *necessarily* produced the claimed invention's features.
[2] *Motorola, Inc. v. Interdigital Technology Corp.*, 43 USPQ2d 1481 (Fed. Cir. 1997)
[3] *Ex parte Levy*, 17 USPQ2d 1461, 1464 (Bd.Pat.App.& Inf. 1990)

domain interaction. Disruption of apoE4 domain interaction would not be expected to lower apoE4 levels in the CNS. Applicants have not elucidated a mechanism of action. Accordingly, the statement that a "mechanism of action of a treatment does not have a bearing on the patentability of the invention" is irrelevant to the instant case.

Conclusion as to the rejection under 35 U.S.C.§102(a)

Applicants submit that the rejection of claims 1-4 and 19-22 under 35 U.S.C. §102(a) has been adequately addressed in view of the remarks set forth above. The Examiner is thus respectfully requested to withdraw the rejection.

III. CONCLUSION

Applicants submit that all of the claims are in condition for allowance, which action is requested. If the Examiner finds that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-0815, order number UCAL096CIP3.

Respectfully submitted,
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Date: Apr. 27, 2004

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